REMARKS

A. Status of the Claims

Claims 1-51 were pending at the time of the present action. Of these, claims 1-37 and 41-51 have been canceled. Claim 52-99 have been added. Support for the added claims may be found throughout the specification, for example at page 9, lines 24 through page 10, line 14 and page 77, line 23 through page 81, line 29. Therefore, claims 38-40 and 52-99 are currently pending. These claims, as currently pending, are reproduced in Appendix A.

B. Traversal of the Action's Characterization of the Invention

In the Restriction Requirement, the Examiner stated that the methods of the four claim groups are unrelated because "they have different goals, require different reagents and have different methods steps." Specifically, Groups 2 and 3 were distinguished "because while both groups have the goal of reducing the susceptibility of animals to infection . . . Group 2 does so by administering a polypeptide while Group 3 accomplishes this goal using methods for administering polynucleotides."

While the Group 2 and Group 3 claims are not currently elected for prosecution, Applicants respectfully traverse the Action's characterization of these claims as separate inventions. The Action is incorrect in its assertion that the Group 2 claims relate simply to the administration of a "polypeptide," while the Group 3 claims relate simply to the administration of a "polynucleotide." Further, the Examiner has not provided adequate explanation to carry the required burden under MPEP § 803.

The Action notes that the goals of the claims it designates as Group 2 and 3 are identical. The Action further notes the overlap of most of the claims within Group 2 and 3. However, the Action finds that the overlapping claims are "drawn broadly so as to embrace both methods."

The claims grouped by the Action into Group 2 and 3 are all species of the genus claimed by claim 23. Claim 23 reads:

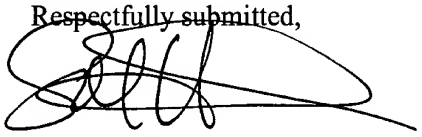
A method of reducing susceptibility of an animal to infection comprising the step of modulating an LPS mediated response in the animal.

All of the claims cited by the Action as falling within group 2 and 3 relate to a method of reducing susceptibility of an animal to infection comprising the step of modulating an LPS mediated response in the animal. The distinction cited by the Action is not supportable and insufficient under MPEP § 803 to establish a *prima facie* case of distinct invention.

The distinction drawn by the Action to "polynucleotide" versus "polypeptide" is applicable only to a narrow construction of the remaining claims. Claims related to regulation of expression may be carried out through the introduction of a polypeptide. Conversely, TLR-4 may be introduced into a cell through the transfection of a host with a polynucleotide expression cassette. The claims are thus not readily distinguishable on the lines drawn by the action. Consequently, the restriction is improper under MPEP § 806(C) because the claims as properly construed are related as disclosed and not distinct as claimed.

The Examiner is invited to contact the undersigned attorney at 512-418-3058 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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[redacted]

APPENDIX A

38. A method of screening for modulators of an LPS mediated response comprising the steps of:

a) obtaining a TLR-4 polypeptide;

b) determining a standard activity profile of the TLR-4 polypeptide;

c) contacting the TLR-4 polypeptide with a putative modulator; and

d) assaying for a change in the standard activity profile.

39. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:98 or SEQ ID NO:99.

40. The method of claim 39, wherein the standard activity profile of the TLR-4 polypeptide is determined by determining the ability of the TLR-4 polypeptide to stimulate transcription of a reporter gene, the reporter gene operatively positioned under control of a nucleic acid segment comprising a promoter from a TLR-4 gene.

52. The method of claim 38, wherein said putative modulator affects the function of TLR-4.

53. The method of claim 52, wherein said putative modulator is an agonist.

54. The method of claim 52, wherein said putative modulator is an antagonist.

55. The method of claim 52, wherein said putative modulator affects the transcription of TLR-4.

56. The method of claim 52, wherein said putative modulator affects the translation of TLR-4.

57. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:2.

58 The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:4.

59 The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:6.

60. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:98.

61. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:99.

62. The method of claim 38, wherein said nucleic acid segment and putative modulator are maintained under conditions that normally allow for TLR-4 transcription and translation.

63. The method of claim 38, wherein said putative modulator inhibits TLR-4 directed signaling of TNF secretion.

64. The method of claim 38, wherein said putative modulator stimulates TLR-4 directed signaling of TNF secretion.

65. The method of claim 38, wherein said putative modulator to be screened is obtained from a library of synthetic chemicals.

66. The method of claim 38, wherein said putative modulator to be screened is obtained from a natural source.

67. The method of claim 65, wherein said natural source is selected from the group consisting of animals, bacteria, fungi, plant sources and marine samples.

68. The method of claim 38, wherein said putative modulator to be screened is a protein or peptide.

69. The method of claim 38, wherein said putative modulator to be screened is a small molecule inhibitor.

70. The method of claim 38, wherein said putative modulator to be screened is a nucleic acid molecule.

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71. The method of claim 38, wherein said putative modulator to be screened is a stimulator of an immune response.

72. The method of claim 71, wherein said stimulator of an immune response is a cytokine.

73. The method of claim 71, wherein said stimulator of an immune response is an interferon.

74. The method of claim 38, wherein said TLR-4 polypeptide is encoded by a nucleic acid sequence selected from the group comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:46, SEQ ID NO:47 and SEQ ID NO:48.

75. The method of claim 38, wherein said putative modulator to be screened is an IL-1 receptor antagonist.

76. The method of claim 38, wherein said putative modulator to be screened is selected based upon a knowledge of the TLR-4 protein structure.

77 A method of screening for modulators of an LPS mediated response comprising the steps of:

(i) providing a TLR-4 polypeptide;

(ii) determining a standard activity profile of said TLR-4 polypeptide;

(iii) contacting said TLR-4 polypeptide with a candidate substance; and

(iv) comparing activity of the TLR-4 polypeptide contacted with said candidate substance with the standard activity profile,

wherein a change in the activity of the TLR-4 polypeptide contacted with the candidate substance, when related to the standard activity profile, indicates that said candidate substance is a modulator of an LPS mediated response.

78. The method of claim 77, wherein the standard activity profile of the TLR-4 polypeptide is determined by determining the ability of the TLR-4 polypeptide to stimulate transcription of a reporter gene, the reporter gene operatively positioned under control of a nucleic acid segment comprising a promoter from a TLR-4 gene.

79. The method of claim 77, wherein said candidate substance affects the function of TLR-4.

80. The method of claim 79, wherein said candidate substance is an agonist.

81. The method of claim 79, wherein said candidate substance is an antagonist.

82. The method of claim 79, wherein said candidate substance affects the transcription of TLR-4.

83. The method of claim 79, wherein said candidate substance affects the translation of TLR-4.

84. The method of claim 77, wherein the TLR-4 polypeptide has the amino acid sequence selected from the group comprising SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:98 and SEQ ID NO:99.

85. The method of claim 77, wherein said nucleic acid segment and candidate substance are maintained under conditions that normally allow for TLR-4 transcription and translation.

86. The method of claim 77, wherein said candidate substance inhibits TLR-4 directed signaling of TNF secretion.

87. The method of claim 77, wherein said candidate substance stimulates TLR-4 directed signaling of TNF secretion.

88. The method of claim 77, wherein said candidate substance to be screened is obtained from a library of synthetic chemicals.

89. The method of claim 77, wherein said candidate substance to be screened is obtained from a natural source.

90. The method of claim 89, wherein said natural source is selected from the group consisting of animals, bacteria, fungi, plant sources and marine samples.

91. The method of claim 77, wherein said candidate substance to be screened is a protein or peptide.

92. The method of claim 77, wherein said candidate substance to be screened is a small molecule inhibitor.

93. The method of claim 77, wherein said candidate substance to be screened is a nucleic acid molecule.

94. The method of claim 77, wherein said candidate substance to be screened is determined to be a stimulator of an immune response.

95 The method of claim 94, wherein said stimulator of an immune response is a cytokine.

96. The method of claim 94, wherein said stimulator of an immune response is an interferon.

97. The method of claim 77, wherein said TLR-4 polypeptide is encoded by a nucleic acid sequence selected from the group comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:46, SEQ ID NO:47 and SEQ ID NO:48.

98. The method of claim 77, wherein said candidate substance to be screened is an IL-1 receptor antagonist.

99. The method of claim 77, wherein said candidate substance to be screened is selected based upon a knowledge of the TLR-4 protein structure.